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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/701,626	12/01/2000	Elisabeth A. Raleigh	NEB-165-PUS	8938

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EXAMINER
CHAKRABARTI, ARUN K

ART UNIT	PAPER NUMBER
1634	13

DATE MAILED: 12/27/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/701,626	Raleigh
Examiner	**Art Unit**
Arun Chakrabarti	1634

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Dec 10, 2002* .

2a) ☒ This action is **FINAL.** 2b) ☐ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☒ Claim(s) *7-14 and 17* is/are allowed.

6) ☒ Claim(s) *1-6 and 18-20* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☒ Claims *15 and 16* are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *Detailed Action*

DETAILED ACTION

Specification

1. Claims 1 and 2 have been amended and new claims 18-20 have been added.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 1-6 and 18-20 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-6 and 18-20 are rejected over the recitation of the phrase, "cloning the **on** or more genes" in step C) of claim 1. It is not clear if a new gene named "**on**" (which does not have a basis in the specification or claim) is claimed or "one" is claimed or both are claimed. The metes and bounds of the claims are vague and indefinite.

Claim Rejections - 35 USC § 102

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

5. Claims 1, 5, and 6 are rejected under 35 U.S.C. 102 (b) as being anticipated by Silver et al. (U.S. Patent 4,994,370) (February 19, 1991).

Silver et al teaches a method for the cloning of intact, diversity-selected genes from within gene cassettes, the method comprising the steps of:

a) identifying repeat DNA sequences in the cassette array (Figure 4, step 1);

b) hybridizing oligonucleotides to the repeated sequences which flank the gene cassettes and amplifying the sequences to provide DNA fragments which contain genes from within the cassettes (Figure 4, steps II and III).;

c) inherently ligating the DNA fragments into a vector (Column 7, lines 13-16 and Column 8, lines 26-28);

d) transforming the vector into an appropriate strain (Column 8, lines 26-28).

Silver et al teaches a method, wherein the oligonucleotides contain recognition sites which permit directional cloning (Column 7, lines 13-16).

Silver et al inherently teaches a method, wherein the DNA fragments are ligated into the vector in an orientation that enables expression (Column 8, lines 26-28).

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CAR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103© and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

7. Claims 2 and 18 are rejected under 35 U.S.C. 103 (a) over Russell et al. (U.S. Patent 6,312,944 B1) (November 6, 2001) in view of Silver et al. (U.S. Patent 4,994,370) (February 19, 1991).

Russell et al. teaches a method of cloning the diversity-selected genes comprising adhesin peptides fimbrial protein genes (Abstract and Example, and Example 2).

Russell et al. does not teach a method for cloning according to claim 1.

Silver et al. teach a method for cloning according to claims 1-2 as described above.

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to substitute and combine the method of cloning of Silver et al. in the method of cloning the diversity-selected genes comprising adhesin peptides fimbrial protein genes of Russell et al. since Silver et al. state, "While standard cloning techniques could be

used to obtain the same results, the "inside-out" PCR method is substantially superior, yielding purified "junction" fragment DNA in a single day, compared to a few weeks for standard cloning (Column 9, lines 36-40)". By employing scientific reasoning, an ordinary practitioner would have been motivated to substitute and combine the method of cloning of Silver et al. in the method of cloning the diversity-selected genes comprising adhesin peptides fimbrial protein genes of Russell et al. in order to achieve the express advantages, as noted by Silver et al., of a cloning technique which is substantially superior, yielding purified "junction" fragment DNA in a single day, compared to a few weeks for standard cloning.

8. Claim 3 is rejected under 35 U.S.C. 103 (a) over Xu (U.S. Patent 5,492,823) (February 20, 1996) in view of Silver et al. (U.S. Patent 4,994,370) (February 19, 1991).

Xu teaches a method of cloning the diversity-selected genes comprising restriction-endonuclease genes (Abstract and Examples 1-5 and Figure 3).

Xu does not teach a method for cloning according to claim 1.

Silver et al. teach a method for cloning according to claim 1 as described above.

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to substitute and combine the method of cloning of Silver et al. in the method of cloning the diversity-selected genes comprising restriction-endonuclease genes of Xu since Silver et al. state, "While standard cloning techniques could be used to obtain the same results, the "inside-out" PCR method is substantially superior, yielding purified "junction" fragment DNA in a single day, compared to a few weeks for standard cloning (Column

9, lines 36-40)". By employing scientific reasoning, an ordinary practitioner would have been motivated to substitute and combine the method of cloning of Silver et al. in the method of cloning the diversity-selected genes comprising restriction-endonuclease genes of Xu in order to achieve the express advantages, as noted by Silver et al., of a cloning technique which is substantially superior, yielding purified "junction" fragment DNA in a single day, compared to a few weeks for standard cloning.

9. Claim 4 is rejected under 35 U.S.C. 103 (a) over Stein et al. (U.S. Patent 5,491,060) (February 13, 1996) in view of Silver et al. (U.S. Patent 4,994,370) (February 19, 1991).

Stein et al. teaches a method of cloning the diversity-selected genes comprising methyltransferase genes (Abstract and Column 2, lines 15-44 and Example).

Stein et al. does not teach a method for cloning according to claim 1.

Silver et al. teach a method for cloning according to claims 1 as described above.

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to substitute and combine the method of cloning of Silver et al. in the method of cloning the diversity-selected genes comprising methyltarnsferase genes of Stein et al. since Silver et al. state, "While standard cloning techniques could be used to obtain the same results, the "inside-out" PCR method is substantially superior, yielding purified "junction" fragment DNA in a single day, compared to a few weeks for standard cloning (Column 9, lines 36-40)". By employing scientific reasoning, an ordinary practitioner would have been motivated to substitute and combine the method of cloning of Silver et al. in the method of cloning the

diversity-selected genes comprising methyltransferase genes of Stein et al. in order to achieve the express advantages, as noted by Silver et al., of a cloning technique which is substantially superior, yielding purified "junction" fragment DNA in a single day, compared to a few weeks for standard cloning.

10. Claim 19 is rejected under 35 U.S.C. 103 (a) over Gruber et al. (U.S. Patent 6,495,349 B1) (December 17, 2002) in view of Russell et al. (U.S. Patent 6,312,944 B1) (November 6, 2001) further in view of Silver et al. (U.S. Patent 4,994,370) (February 19, 1991).

Gruber et al. teaches a method of cloning the diversity-selected genes comprising signalling peptide kinases genes (Example 4).

Gruber et al. does not teach a method for cloning according to claims 1-2.

Russell et al in view of Silver et al. teach a method for cloning according to claims 1-2 as described above.

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to substitute and combine the method of cloning of Russell et al in view of Silver et al. in the method of cloning the diversity-selected genes comprising signalling peptide kinases genes of Gruber et al. since Silver et al. state, "While standard cloning techniques could be used to obtain the same results, the "inside-out" PCR method is substantially superior, yielding purified "junction" fragment DNA in a single day, compared to a few weeks for standard cloning (Column 9, lines 36-40)". By employing scientific reasoning, an ordinary practitioner would have been motivated to substitute and combine the method of cloning of

Russell et al in view of Silver et al. in the method of cloning the diversity-selected genes comprising signalling peptide kinases genes of Gruber et al. in order to achieve the express advantages, as noted by Silver et al., of a cloning technique which is substantially superior, yielding purified "junction" fragment DNA in a single day, compared to a few weeks for standard cloning.

11. Claim 20 is rejected under 35 U.S.C. 103 (a) over Coruzzi et al. (U.S. Patent 5,391,725) (February 21, 1995) in view of Russell et al. (U.S. Patent 6,312,944 B1) (November 6, 2001) further in view of Silver et al. (U.S. Patent 4,994,370) (February 19, 1991).

Coruzzi et al. teaches a method of cloning the diversity-selected genes comprising detoxifying enzymes (drug resistant determinant) genes (Column 14, lines 37-51).

Coruzzi et al. does not teach a method for cloning according to claims 1-2.

Russell et al in view of Silver et al. teach a method for cloning according to claims 1-2 as described above.

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to substitute and combine the method of cloning of Russell et al in view of Silver et al. in the method of cloning the diversity-selected genes comprising detoxifying enzymes (drug resistant determinant) genes of Coruzzi et al. since Silver et al. state, "While standard cloning techniques could be used to obtain the same results, the "inside-out" PCR method is substantially superior, yielding purified "junction" fragment DNA in a single day, compared to a few weeks for standard cloning (Column 9, lines 36-40)". By employing scientific

reasoning, an ordinary practitioner would have been motivated to substitute and combine the method of cloning of Russell et al in view of Silver et al. in the method of cloning the diversity-selected genes comprising detoxifying enzymes (drug resistant determinant) genes of Coruzzi et al. in order to achieve the express advantages, as noted by Silver et al., of a cloning technique which is substantially superior, yielding purified "junction" fragment DNA in a single day, compared to a few weeks for standard cloning.

Allowable Subject Matter

12. Claims 7-14, and 17 are allowed because no prior art of record either teaches or suggests the SEQ ID Numbers disclosed in the claims.

Response to Amendment

13. In response to amendment, previous 112 (second paragraph) rejection has been withdrawn. However, a new 112 (second paragraph) rejection and two new 103(a) rejection have been included. 102(b) rejection has been properly maintained.

Response to Arguments

14. Applicant's arguments filed on December 10, 2002 have been fully considered but they are not persuasive.

Applicant argues that 102(b) rejection should be withdrawn because Silver et al does not teach the same order of instant method steps, e.g., ligation precedes amplification in Silver et al whereas in instant claims amplification (step b) precedes ligation (step c). This argument is not persuasive. In presence of "comprising" language of the instant claim 1, any extra step(s) or material(s) can be added in between steps (a) and (b). It is hereby mentioned that open "comprising" language allows any chemical moieties or steps on the surface of the earth to be attached to the cloning method. MPEP 2111.03 recites, "The transitional term "comprising", which is synonymous with "including", "containing" or "characterized by" is inclusive or open-ended and does not exclude additional, unrelated elements or method steps. *Molecular Research Corp. v. CBS, Inc.*793 F.2d 1261, 229 USPQ 805 (Fed. Cir. 1986); *In re Baxter,* 656 F.2d 679, 686, 210 USPQ 795, 803 (CCPA 1981); *Ex parte Davis,* 80 USPQ 448, 450 (Bd. App. 1948) ("comprising" leaves "the claim open for the inclusion of unspecified ingredients even in major amounts"). Therefore, ligation step preceding amplification, as taught by Silver et al. (102 (b) art), meets all the requirements of the claims. Moreover, applicant is also informed that MPEP 2144.04 further states, " *In re Gibson,* 39 F.2d 975, 5 USPQ 230 (CCPA 1930) Selection of any order of mixing ingredients is *prima facie* obvious".

Applicant argues that Silver reference does not teach the method for analyzing an unknown cell DNA of the claimed invention. This argument is not persuasive. In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., the method for analyzing an unknown cell

DNA environment) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

Applicant then argues the 102 and 103 rejections are improper because it lacks a reasonable expectation of success.

With regard to the "lacks a reasonable expectation of success." argument, The MPEP 2143.02 states , "Obviousness does not require absolute predictability, however, at least some degree of predictability is required. Evidence showing there was no reasonable expectation of success may support a conclusion of nonobviousness. In re Rinehart , 531 F.2d 1048, 189 USPQ 143 (CCPA 1976) (Claims directed to a method for the commercial scale production of polyesters in the presence of a solvent at superatmospheric pressure were rejected as obvious over a reference which taught the claimed method at atmospheric pressure in view of a reference which taught the claimed process except for the presence of a solvent. The court reversed, finding there was no reasonable expectation that a process combining the prior art steps could be successfully scaled up in view of unchallenged evidence showing that the prior art processes individually could not be commercially scaled up successfully.). See also Amgen, Inc. v. Chugai Pharmaceutical Co ., 927 F.2d 1200, 18 USPQ2d 1016 (Fed. Cir.), cert. denied , 502 U.S. 856 (1991) (In the context of a biotechnology case, testimony supported the conclusion that the references did not show that there was a reasonable expectation of success. 18 USPQ2d at 1022, 1023.); In re O'Farrell , 853 F.2d 894, 7 USPQ2d 1673, 1681 (Fed. Cir. 1988) (The court held the claimed method would

have been obvious over the prior art relied upon because one reference contained a detailed enabling methodology, a suggestion to modify the prior art to produce the claimed invention, and evidence suggesting the modification would be successful.)."

There is no evidence of record submitted by applicant demonstrating the absence of a reasonable expectation of success. There is evidence in the Silver reference of the enabling methodology, the suggestion to modify the prior art, and evidence that a number of different DNA strands were actually experimentally studied and found to be functional (METHODS I and II). This evidence of functionality trumps the attorney arguments, which argues that Silver reference is an invitation to research, since Silver steps beyond research and shows the functional product.

In view of the response to arguments and amendments, 102(b) rejection has been properly maintained and two new 103(a) rejections have been properly included.

Conclusion

15. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CAR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period

will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CAR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Arun Chakrabarti, Ph.D. whose telephone number is (703) 306-5818.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones, can be reached on (703) 308-1152.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group analyst Chantae Dessau whose telephone number is (703) 605-1237.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission via the P.T.O. Fax Center located in Crystal Mall 1. The CM1 Fax Center numbers for Technology Center 1600 are either (703) 305-3014 or (703) 308-4242. Please note that the faxing of such papers must conform with the Notice to Comply published in the Official Gazette, 1096 OG 30 (November 15, 1989).

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December 19, 2002